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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/989,725
Filing Date: November 20, 2001
Appellant(s): ASHKENAZI ET AL.

Daphne Reddy
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 30 May 2006 appealing from the Office action mailed 15 November 2004.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The claims pending in the current application are directed to a nucleic acid encoding a polypeptide that is referred as "PRO1375". There exists one related patent application, U.S. Serial No. 09/997,573, filed on November 15, 2001 (containing claims directed to said PR01375 polypeptides), which has been appealed.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is essentially correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows: Claims 119-124, 127, 132 are also rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement.

(7) Claims Appendix

A substantially correct copy of appealed claims 119-127, 129-132 and 134-138 appears on pages 29-33 of the Appendix to the appellant's brief of 30 May 2006.

(8) Evidence Relied Upon

The following is a listing of the evidence (e.g., patents, publications, Official Notice, and admitted prior art) relied upon in the rejection of claims under appeal.

a) Kahan, Current Opinion in Immunology. 4: 553-560, 1992.

b) Piccotti et al., Transplantation, 67 (11): 1453-1460, 1999.

c) Campo, et al., Biol. Trace Element Res., 79: 15-22, 2001.

d) Nishioka et al. Journal ofLeukocyte Biology, Vol.73, pages 621-219, 2003.

e) Current Protocols in Immunology, Vo.1, Richard Coico, Series Ed, John Wiley & Sons, Inc. 1991, Unit 3.12.

f) Gubler et al., PNAS 88 : 4143-4147, 1991. (cited by Appellant)

g) Peterson et al., J. Clinical Oncology 21412) : 2342-2348, 2003. (cited by Appellant)

h) Thurner et al., J. Experimental Medicine, 190(11) : 1669-1678, 1999. (cited by Appellant)

i) Steinman et al. Drug News Perspect. 13(10): 581-586, 2000. (cited by Appellant)

j) US Patent No. 5,817,306 HASKILL et al. 10-1998 (newly cited by Examiner).

Priority:

The grounds of rejection in the instant application are a direct result of the determination of priority for the claimed subject matter. Appellant asserts priority of the instant application to Provisional Application 60/144,758, filed 20 July 1999. However,

priority has not been granted to this earlier application. Based on the invention given by Appellant and an inspection of the patent applications, the Examiner has concluded that the subject matter defined in this application is not supported by the disclosure 60/144,758, filed 07/20/1999 because said parent application, does not satisfy the enablement requirement under 35 U.S.C. §112, first paragraph, of how to use the claimed invention.

Accordingly, the subject matter defined in claims 119-127, 129-132 and 134-138 is afforded an effective filing date of 11/20/2001, which is the filing date of the current application.

(9a) Grounds of Rejection

Claim Rejections - 35 U.S.C. §101, §112, first paragraph :

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following grounds of rejection are applicable to the appealed claims:

(It is noted that claim 134 depends from a cancelled claim, accordingly, claim 134 is objected to). Claims 119-127, 129-131 and 135-138 are directed to an isolated nucleic acid having at least 80%, 85%, 90%, 95%, and 99% sequence identity to (a) a nucleic acid encoding the polypeptide of SEQ ID NO:418, (b) a nucleic acid sequence

encoding the polypeptide of SEQ ID NO:418, lacking its associated signal peptide, (c) a nucleic acid sequence encoding the extracellular domain of the polypeptide of SEQ ID NO:418, (d) a nucleic acid of SEQ ID NO:417, (e) the full-length coding sequence of the nucleic acid of SEQ ID NO:417 or (f) the full-length coding sequence of the cDNA deposited under ATCC accession number 203115; wherein the polypeptide encoded by aid nucleic acid induces proliferation of stimulated T lymphocytes in a mixed lymphocyte reaction.

Claims 119-127, 129-131 and 134-138 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. Claims 119-127, 129-131 and 135-138 are also rejected under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is not supported by either a substantially asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Appellant asserts that the specification shows that PRO1375 polypeptide encoded by the claimed nucleic acid stimulates an immune response and induces inflammation in the skin vascular permeability assay. However, while the VP assay might indicate that PRO1375 is an inflammatory cytokine (although based on such a result, the person of ordinary skill in the art would not consider that to be a supportable conclusion), it might alternatively indicate that the guinea pigs are allergic to PRO1375, e.g. that the human PR01375 protein has an epitope that the guinea pigs were pre-sensitized to, or even just that it is an irritant, similar to lye (which would give a similar

response in the assay). Thus, it does not appear that the VP assay provides a real-world, readily available use. It should be made clear that Appellant is not appealing this assertion. Appellant's ground of appeal deals with whether the MLR assay (Example 151) satisfies the utility requirement set forth in 35 U.S.C §101 or "how to use" prong of the enablement under 35 U.S.C §112.

The instant specification discloses that the protein encoded by the claimed nucleic acid (PRO1375 - SEQ ID NO:418) tested positive in the MLR assay wherein "positive increases over control are considered positive with increases of 180% or greater over control" (see pages 525, lines 29-33 of the specification).

It was previously asserted by the Examiner that insufficient evidence was provided to support the position that the MLR assay was an art recognized *in-vitro* assay that was predictive of general immune responses *in-vivo*. Several references were cited during the prosecution of the instant application which demonstrated either a showing that the results of the MLR assay were consistent with in vivo activity or were inconsistent with in vivo activity. Upon review of the prior art, the Examiner found a patent that states "The mixed lymphocyte response (MLR) and phytohemagglutinin A (PHA) assays are valuable for identifying immune suppressive molecules *in-vitro* that are useful for treating graft versus host disease. The results obtained from these assays are generally predictive of their *in-vivo* effectiveness." (See column 12, lines 36-41 of US Patent No. 5,817,306). Therefore, it is conceded that the MLR assay is art recognized for identifying molecules, which suppress an immune response. However, another basis for rejecting the claims for lack of utility has been the lack of support in

the specification for the assertion that the polypeptide of the instant claims actually stimulates the proliferation T- lymphocytes. In Example 151 on page 525, it is stated that "positive increases over control are considered positive however, increases of greater than or equal to 180% being preferred. However, any value greater than control indicates a stimulatory effect for the test protein", (see page 525, lines 29-33). The specification does not provide any values or data for the proteins tested in the assay. The specification provides no information at all regarding the results of the assay except that a certain protein tested positive and the statement that "any value more than control indicates an stimulatory effect for the test protein'. If the claimed invention is to be used for therapeutic enhancement of the immune response of an individual, the question to ask is how are the results of the MLR assay related to the asserted utility of the claimed invention? The previous Office actions go into great depth regarding the nature of the MLR assay and how those skilled in the art use this assay and what kind of determinations can be made about compounds which are tested in this assay. The MLC (a.k.a. MLR) assay is a measure of alloreactivity of one individual to another individual. This reactivity is governed by the antigenic disparity between the two individuals which are being compared in the assay. This reactivity is governed by the antigenic disparity between the two individuals which are being compared in the assay. Depending on the individuals being tested, the MLC may indicate stimulation if they are HLA-disparate or the MLC may indicate no stimulation if the individuals are HLA-identical. The ability of the claimed invention to stimulate proliferation in the MLC assay may not be a general stimulus to lymphocyte proliferation, but rather a reaction to one

of the MHC antigens on the responder cell. The instant specification fails to provide sufficient detail of the assay which was performed and fails to provide any data whatsoever in order for one of ordinary skill in the art to evaluate the conclusion that lymphocyte proliferation was stimulated by the claimed invention. Furthermore, there is known inherent variability of individual cellular responses from day to day, which would clearly dictate the need for internal controls. The specification indicates that CD4-IgG was used as a control, but it is not clear how this should control for background stimulation or provide for a measure of maximal stimulation. Lastly, the specification fails to provide any data or evidence of the results of the assay, therefore, one of ordinary skill in the art cannot evaluate the conclusion of the specification. The specification states that "positive increases over control are considered positive", however, this does not indicate that statistical significance must occur for determination of a positive result in the assay and therefore, the polypeptide in question may not alter the proliferation of stimulated T- lymphocytes to a significant extent. In conclusion, the results of the MLC (a.k.a. MLR) assay as disclosed in the specification for the polypeptide PRO1375 do not support a specific and substantial utility for the claimed invention because one of ordinary skill in the art would not conclude that a molecule which tested positive in the assay of the specification wherein any increases over control is considered to be a positive result, would be useful as a molecule for therapeutically stimulating an immune response in an individual (asserted use). There is insufficient data presented, as well as insufficient controls used, to conclude anything regarding the ability of the claimed polypeptide to be used in a substantial way to

therapeutically inhibit the immune response of an individual, and further experimentation would be required to use the invention in this manner.

(10a) Response to Argument

Appellant argues, beginning at page 6 of the Brief, that the reference cited by the Examiner to show that there is no correlation between the ability to stimulate proliferation of lymphocytes in the MLR in vitro assay and that same ability in vivo, i.e Kahan et al., Piccotti et al., and Campo et al., are insufficient to make the prima facie case. However, as stated above, the disclosure of newly cited US Patent No. 5,817,306 establishes the state of the art at the time the invention was made that the results of the MLR assay are generally predictive of in vivo effects. Therefore, arguments directed to the correlation or predictive nature of the MLR assay are moot and will not be addressed further. However, arguments are directed toward the disclosure of the specification and the conclusion that can be made from said disclosure will be addressed since they are critical to the holding of lack of utility for inhibition of T-lymphocyte proliferation by the claimed polypeptide.

At pages 5 and 12-13 of the Brief, Appellant discusses the Declaration submitted by Dr. Sherman on Fong 5 August 2004. This declaration has been fully considered, but not found to be persuasive. Dr. Fong concludes "a PRO polypeptide shown to stimulate T-cell proliferation in the MLR assay where the activity is observed as 180% over control, as specified in the present application, would be expected activity as that exhibited by IL-12, and would therefore find practical utility as an immune stimulation". In assessing the weight to be given expert testimony, the Examiner may properly

consider, among other things, the nature of the fact sought to be established, the strength of any opposing evidence, the interest of the expert in the outcome of the case, and the presence or absence of factual support for the expert's opinion. See & parte Simnson, 61 USPQ2d 1009 (BPAI 2001), Cf. Redac Inrl. Ltd. v. Lotus Develonment Corn., 81 F.3d 1576, 38 USPQ2d 1665 (Fed. Cir. 1996), Paranon Podiatrv Lab.. Inc. v. KLM Lab., Inc., 948 F.2d 1 182, 25 USPQ2d 1561, (Fed. Cir.1993). In the instant situation, the nature of the fact sought to be established is whether or not the disclosure that PRO1375 tested "positive" in the MLR assay of Example 151 supports the assertion that it could be used to stimulate proliferation of T-lymphocytes and therefore, be used for therapeutic enhancement of the immune system. Dr. Fong's statement that the present invention has an activity of at least 180% is questioned because there is no data presented to support this conclusion. The specification may state that increases of greater than or equal to 180% are preferred, but there is no disclosure, in the specification or in any other source, that the alleged increase reported in the specification for the claimed protein was of any particular degree. The only conclusion that can be made from the evidence provided for the claimed protein of PRO1375 is that the increase was a value greater than control since this was the standard provided for determination of a positive increase. The significance of this conclusion can be questioned since proper assay controls, deemed essential in the art were not used and because the standard for determination of a positive response in the assay would not be accepted by those of skill in the art (statistical significance is the standard for evaluating therapeutic value of a compound). The expert has interest in the outcome of the case

since Dr. Fong is listed as an inventor and is employed by the assignee. Finally, the expert refers to Gubler et al. as factual support for the conclusions in the declaration. However, Gubler et al. do not appear to indicate that a protein shown to stimulate T-cell proliferation in an MLR assay with an activity of at least 180% would be expected to have the type of activity as that exhibited by IL-12. Furthermore, Gubler et al. (as well as Peterson et al. and Thurner et al.) are silent to any activity possessed by the claimed protein. The Fong declaration evinces that the instant specification provides a mere invitation to experiment, and not a readily available utility. The PRO1375 protein has not been shown to therapeutically enhance the immune system. The specification merely demonstrates that the PRO1375 protein increases T-cell proliferation above control. It is not known whether this increase is significant or what the relative increase in proliferation is. In the absence of any of the above information, all that the specification does is present evidence that the PRO1375 protein may increase T-cell proliferation and invites the artisan to determine the significance of this increase and whether it is meaningful (i.e. useful for a therapeutic benefit). It remains that the specification is not sufficient to conclude anything about the nature of the activity of the PRO1375 protein. Based on consideration of the evidence as a whole, the finding of lack of utility based on the MLR assay of Example 151 is proper.

Appellant argues at page 9 of the Brief that the instant application claims priority to an earlier filed application (60/144,758, filed 20 July 1999) and that they are entitled to benefit to this earlier filed application based on the disclose that PRO1375 tested positive in the MLR assay. As pointed out in the grounds of the rejection, this is an issue

to be addressed in this Appeal. If the disclosure in the specification is deemed sufficient to provide utility for the claimed invention based on the asserted use for therapeutic stimulation of an immune response, then Appellant is entitled to the effective filing date of the 60/144,758 application. However, priority has been denied because the disclosure has been found insufficient to establish this utility for the claimed invention.

At pages 9-12, Appellant reviews case law pertaining to the legal standard for patentable utility, with which the Examiner does not take issue. At page 11, Appellant asserts that the phrase "immediate benefit to the public" does not necessarily have to mean the invention is "currently available" to the public in order to satisfy utility requirements. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a 'substantial' utility." (MPEP § 2170.01).

This argument has been fully considered, but is not persuasive. MPEP §2170.01 also states that when "further research is required to reasonably confirm the asserted utility, the claims do not meet the requirements of 35 USC 101." In the instant situation, further research would be required to reasonably confirm that the claimed protein stimulates T-cell proliferation to a degree that it would be useful therapeutically for stimulating an immune response, which is the asserted utility in the specification.

At pages 14-15 of the Brief, Appellant argues that the standard for utility is "more likely than not" and that the asserted utility is specific and substantial and that the Examiner "has misinterpreted the focus of the assay disclosed in the specification". Appellant's argument has been fully considered, but is not persuasive. The question of

whether the art recognizes the MLR assay as predictive of in vivo therapeutic value has been answered. However, the specification does not support the conclusion that the protein (PRO1375), encoded by the claimed nucleic acid stimulates proliferation of T-lymphocytes such that it would have therapeutic application for enhancing the immune response. As pointed out previously, no data is presented and the statement that proliferation was greater than control is not sufficient for concluding that the claimed protein would be useful for a therapeutic application, which is the asserted utility based on this assay. The assay relied upon in the instant specification is deficient in that proper art-recognized controls are not present, measured values of stimulation are not present, variability is not disclosed, statistical significance is not disclosed, such that an independent evaluation and conclusion cannot be made. One skilled in the art would have to do further research to determine whether or not the increase in T-cell proliferation by PRO1375 polypeptide in the MLR assay is real and significant, and therefore, support the asserted use for therapeutic enhancement of immune response. Such further research requirements make it clear that the asserted utility is not yet in currently available form, ie-, it is not substantial. This further experimentation is part of the act of invention and until it has been undertaken, Appellant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in Brenner F. Mansoni 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "lulnless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "lilt is not a reward for the search, but

compensation for its successful conclusion."

Appellant states at page 12 of the Brief "[t]he positive result for PRO1375 in the MLR assay, described in Example 151, of the specification, demonstrates that PRO1375 is active as a stimulator of the proliferation of stimulated T-lymphocytes".

Appellant's assertion is noted, but the facts of record and the disclosure of the specification do not support this conclusion. As pointed out previously, the specification indicates that "positive increases over control are considered positive", yet art recognized controls, which are considered to be necessary for determining a meaningful result, are not present. The specification fails to include any values which were obtained from the assay, so the results of the assay cannot be independently evaluated. If the degree of stimulation is greater than the control, but within the variability of the assay, then one of ordinary skill in the art would not conclude that the protein tested is a stimulator of T-cell proliferation, yet the specification would arrive at this conclusion. In order to be useful in the manner asserted in the specification (i.e. therapeutic enhancement of an immune response), the degree of stimulation of T-cell proliferation must be meaningful. One of ordinary skill in the art would usually evaluate this by observing a statistically significant increase in T-cell proliferation over baseline. However, based on the limited disclosure in the instant specification, no conclusions can be made as to the activity of the claimed protein in this assay because proper controls are not provided and there is no data presented to evaluate. Therefore, further research would be required to reasonably confirm the asserted utility based on the MLR assay of Example 151.

Appellant's statements and arguments (pages 15-17) directed to use of the MLR to evaluate compounds for use as immunomodulators is noted. However, in view of the Examiner's concession that the MLR is an art accepted assay for this purpose, these arguments are moot.

Appellant again refers to the Declaration of Dr. Fong at pages 13-14 of the Brief. As stated previously, the Declaration has been fully considered but is not persuasive. Appellant asserts that the "specification clearly discloses that PRO1375 tested positive inthe MLR assay" and that the "Fong Declaration reinforces the teachings of the specification that a PRO polypeptide with an activity in the MLR assay of at least 180% of the control is expected to have the type of activity exhibited by IL-12, and would therefore find practical utility as an immune stimulant" (see page 14 of the Brief).

First, the statement that PRO1375 tested positive in the MLR assay is addressed above. The standard set forth in the specification that "positive increases over control are considered positive" is neither art accepted nor indicative of a meaningful increase in T-cell proliferation. Lacking proper controls and no data, the observation that PRO1375 tested "positive" is meaningless. All assays have variability and the observed increase over control may be natural variation in the assay, and therefore, not an indication of an immunostimulatory effect. Secondly, there is no disclosure that the PRO1375 protein of the instant invention has an activity in the MLR assay of at least 180%, therefore, no conclusions regarding it's activity can be made and one would not conclude that it would have practical utility as an immune stimulant. The Declaration of Dr. Fong is not specific to the claimed protein, PRO1375. The Declaration provides no

data related to the claimed protein, PRO1375. Furthermore, the opinion of Dr. Fong that "a PRO polypeptide shown to stimulate T-cell proliferation in the MLR assay of the present invention with an activity of at least 180% of the control is expected to have the type of activity as that exhibited by IL-12" is not supported by any facts or evidence of record. The references cited do not support this opinion and it is not clear how Dr. Fong arrived at this conclusion. There is no evidence of record which correlates an activity of at least 180% of control as predictive of an activity of IL-12 and there is no comparison of the claimed invention with IL-12. One of ordinary skill in the art would not conclude that the claimed protein has the activity of IL-12 because there is absolutely no data provided to support such an assertion. Therefore, the Declaration is not persuasive to overcome the holding of a lack of utility for the claimed invention based on the MLR assay. Appellant's arguments spanning page 16-25 are directed to use of the MLR to evaluate compounds for use as immunomodulators is noted. However, in view of the Examiner's concession that the MLR is an art accepted assay for this purpose, these arguments are moot. Appellant cites case law concerning the Examiner's requirement to consider all of the evidence of record anew, and that opinion evidence must be considered. Appellant also points to the utility guidelines as directing the Examiner to accept an opinion from an expert. Appellant points to the statement in the Fong declaration that it is Dr. Fong's considered scientific opinion that "a PRO polypeptide shown to stimulate T-cell proliferation in the MLR assay of the present invention with an activity of at least 180% of the control is expected to have the type of activity as that exhibited by IL-12, and would therefore find practical utility as an immune stimulant". At

page 24 Appellant argues that Nishioka et al reference provides supportive evidence for the Appellant's position that the art as a whole recognizes the MLR assay is in fact a widely used in vitro assay for identifying immunomodualtory compounds.

The Examiner has conceded the fact that the MLR assay is art recognized for identifying molecules which suppress an immune response, (See column 12, lines 36-41 of US Patent No. 5,817,306). However, another basis for rejecting the claims for lack of utility has been the lack of support in the specification for the assertion that the polypeptide of the instant claims actually stimulates the proliferation T- lympohcytes.

Appellant argues at page 24 of the Brief that the claims are enabled for the same reasons as provided for utility. However, since the arguments were not persuasive for Supporting utility, they are also not persuasive for supporting enablement. Because the claimed invention does not have utility for therapeutic enhancement of an immune response, and because the specification does not support the conclusion that PRO1375 stimulates T-lymphocytes based on an unreasonable standard for assessing activity and lack of proper experimental controls, the claims are also not enabled for protein

variants that stimulate proliferation of T-lymphocytes. Appellant argues that the claimed nucleic acid variants all share the functional recitation that "wherein the polypeptide encoded by said nucleic acid induces proliferation of stimulated T lymphocytes in a mixed lymphocyte reaction." One skilled in the art could test whether a PRO1375 polypeptide encoded by the claimed variant nucleic acid is capable of stimulating proliferation of T-lymphocytes.

This argument has been considered but it is not persuasive. The specification has not provided sufficient evidence to support the assertion that the polypeptide encoded by the claimed nucleic acid, is capable of stimulating proliferation of T-lymphocytes. Therefore, the claimed invention does not have utility for stimulating proliferation of T-lymphocytes for the reasons provided above, and likewise, the claims are not enabled for this use. Accordingly, since the PRO1375 protein is not enabled, the claimed nucleic acid variants are also not enabled.

(9b) Grounds of Rejection

Claims 119-124, 127, 132 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 119-123 are directed to an isolated nucleic acid having at least 80%, 85%, 90%, 95%, 99% sequence identity to the nucleic acid sequence of SEQ ID NO:417, or to a nucleic acid encoding the polypeptide of SEQ ID NO: 418, wherein said polypeptide induces proliferation of T lymphocytes in a mixed lymphocyte reaction, and claim 132 is drawn to a nucleic acid which hybridizes to the nucleic acid sequence of SEQ ID NO:417, or to a nucleic acid encoding the polypeptide of SEQ ID NO: 418, under the recited hybridization conditions. However, the specification teaches only the structure of the nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO:417 encoding the polypeptide of SEQ IDNO: 418. The specification does not teach functional or structural characteristics of

all the claimed nucleic acids. Claims 124 and 127 recite a nucleic acid encoding the amino acid sequence of the extracellular domain of the polypeptide of SEQ ID NO:418, however, the instant specification does not describe the structure of said extracelular domain or nucleic acid encoding such. The description of one nucleic acids (SEQ ID NO:417) encoding the polypeptide comprising the amino acids set forth in SEQ ID NO: 418, is not adequate written description of an entire genus of functionally equivalent polypeptides. Therefore, the claims do not require that the claimed nucleic acids possess any particular conserved structure, or other disclosed distinguishing feature to retain the desired biological activity. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity without any guidance as to which positions of the polypeptides would tolerate changes to retain the desired biological activity. There is not identification of any particular portion of the structure that must be conserved.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The

specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF'S were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the isolated polypeptide comprising the nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO:417, encoding the polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 418, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

(10b) Response to Argument

Appellant filed no response regarding this rejection.

(9c) Grounds of Rejection:

Claim Rejections - 35 U.S.C. §102(b):

5a. Claims 119-127, 129-132 and 135-138 stand rejected under U.S.C. § 102(b) as being anticipated by MILLENNIUM BIOTHERAPEUTICS INC, (MILL), (WO 00/18904 June/2000); GENENTECH INC. (GETH), (WO 99/63088, September/1999); INCYTE (INCY), (WO 00/00610, June/2000); SAGAMI CHEM RES CENT (SAGA), (WO 00/00506, June/2000). Claims 119-125, 127 and 129-132, 134-138 stand rejected under 35 U.S.C § 102(a) as being anticipated by HELIX RES IST. (HELI), (EP 1130094, September/2001).

The instant claims 119-127, 129-132, 135-138 are drawn to nucleic acid at least 80%, 85%, 90%, 95%, 99% or 100% sequence identity to the nucleic acid encoding the polypeptide of SEQ ID NO: 418, a vector comprising said nucleic acid and a host cell comprising said vector.

Each of references, WO 00/18904, WO 99/63088, WO 00/00610, WO 00/00506 and EP 1130094, discloses an isolated polypeptide that shares 100% amino acid sequence identity to the amino acid sequence of the polypeptide of SEQ ID NO:418, recited in claims 119-127, 129-138 of the instant application, a vector comprising said nucleic acid and a host cell comprising said vector. Regarding claim 131, it is understood that the deposited sequence encodes the polypeptide of SEQ ID NO:418, therefore, since the nucleic acid disclosed by each of the above references encodes a polypeptide that shares 100% identity to the polypeptide of SEQ ID NO:418, these references also anticipate claim 131. With respect to claim 132, the nucleic acid disclosed by each of the references would be expected to hybridize to the complement

of the claimed nucleic acid. With respect to claim 126, the WO 99/6308 discloses a nucleic acid which encodes to the polypeptide of SEQ ID NO:418, lacking its associated signal peptide, (see claim 26 of the world patent WO 99/6308).

Therefore the MILL, GETH, INCY and SAGA references, all anticipate the instant claims 119-127, 129-132,134-138 in the absence of any evidence to the contrary.

(10c) Response to Argument

Appellant argues the rejection of claims 119-127, 129-132 and 135-138, based on the prior art of (WO 00/18904 June/2000), (WO 99/63088, September/1999), (WO 00/00610, June/2000), (WO 00/00506, June/2000) and (EP 1130094, September/2001).

Essentially, Appellant contends that priority to provisional application 60/144,758 should be granted because the MLR assay was first disclosed in this application, and the MLR assay supports utility and meets the requirements of 35 U.S.C.§112 for the subject matter of the instant claims. However, because the arguments regarding utility based on this assay have not been found persuasive for the reasons provided above, the instant application is not entitled to benefit of this earlier filed application. Therefore, the effective filing date is the filing date of current application, which is 11/15/2001.

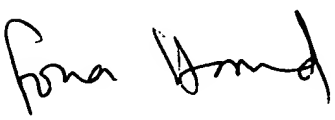
(11) Related Proceedings Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Fozia Hamud



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